The Art and Science of Incorporating Cost Effectiveness into Evidence-Based Recommendations for Clinical Preventive Services

Somnath Saha, MD, MPH, Thomas J. Hoerger, PhD, Michael P. Pignone, MD, MPH, Steven M. Teutsch, MD, MPH, Mark Helfand, MD, MS, Jeanne S. Mandelblatt, MD, MPH, for the Cost Work Group of the Third U.S. Preventive Services Task Force

Abstract: As medical technology continues to expand and the cost of using all effective clinical services exceeds available resources, decisions about health care delivery may increasingly rely on assessing the cost-effectiveness of medical services. Cost-effectiveness is particularly relevant for decisions about how to implement preventive services, because these decisions typically represent major investments in the future health of large populations. As such, decisions regarding the implementation of preventive services frequently involve, implicitly if not explicitly, consideration of costs. Cost-effectiveness analysis summarizes the expected benefits, harms, and costs of alternative strategies to improve health and has become an important tool for explicitly incorporating economic considerations into clinical decision making. Acknowledging the usefulness of this tool, the third U.S. Preventive Services Task Force (USPSTF) has initiated a process for systematically reviewing cost-effectiveness analyses as an aid in making recommendations about clinical preventive services. In this paper, we provide an overview and examples of roles for using cost-effectiveness analyses to inform preventive services recommendations, discuss limitations of cost-effectiveness data in shaping evidence-based preventive health care policies, outline the USPSTF approach to using cost-effectiveness analyses, and discuss the methods the USPSTF is developing to assess the quality and results of cost-effectiveness studies. While this paper focuses on clinical preventive services (i.e., screening, counseling, immunizations, and chemoprevention), the framework we have developed should be broadly portable to other health care services.

Medical Subject Headings (MeSH): economic models, costs and cost analysis, cost-benefit analysis, methods, MEDLINE, preventive health services, evidence-based medicine, practice guidelines (Am J Prev Med 2001;20(3S):36–43)

Introduction

At the close of the twentieth century, health care costs in the United States continued to rise steadily, accounting for 13.5% of the gross domestic product in 1998,[1] and debate on health care funding for the aging American population intensified. In this environment, preventive services often compete with one another and with diagnostic- and treatment-oriented care for increasingly constrained resources.[2] While preventive services are often believed to save costs, delivery of most preventive services, with few

From the Evidence-Based Practice Center (Saha, Helfand) and Division of Medical Informatics and Outcomes Research (Helfand), Oregon Health Sciences University; Section of General Internal Medicine, Portland Veterans Affairs Medical Center (Saha, Helfand), Portland, Oregon; Evidence-based Practice Center, Research Triangle Institute and University of North Carolina (Hoerger, Pignone), and Center for Economics Research, Research Triangle Institute (Hoerger), Research Triangle Park; Department of Internal Medicine, University of North Carolina at Chapel Hill (Pignone), North Carolina; Merck & Co., Inc. (Teutsch), West Point, Pennsylvania; Departments of Oncology and Medicine, Georgetown University Medical Center (Mandelblatt), Washington, DC

Address correspondence to: Somnath Saha, MD, MPH, Portland VA Medical Center (P3MED), 3710 SW US Veterans Hospital Rd., Portland, OR 97207. E-mail: sahas@ohsu.edu

Reprints are available from the AHRQ Web site at www.ahrq.gov/clinic/uspstfix.htm, through the National Guideline Clearinghouse (www.guideline.gov), or in print through the AHRQ Publications Clearinghouse at (1-800-358-9295).

Other members of the Cost Work Group of the third U.S. Preventive Services Task Force include: David Atkins, MD, MPH, Agency for Healthcare Research and Quality, Rockville, Maryland; Alfred O. Berg, MD, MPH, University of Washington, Seattle, Washington; Tracy A. Lieu, MD, MPH, Harvard Community Health Plan, Boston, Massachusetts; Cynthia D. Mulrow, MD, MSc, University of Texas Health Science Center, San Antonio, Texas; Harold C. Sox, Jr, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire; and Carolyn Westhoff, MD, MSc, Columbia University, New York, New York.

0749-3797/01/$–see front matter
PII S0749-3797(01)00260-4

exceptions (e.g., some immunizations), incurs net costs.[3]

Cost-effectiveness analyses (CEAs) summarize the expected benefits, harms, and costs of adopting and translating a clinical recommendation into practice.[4] The results of a CEA are typically presented as a ratio of the net costs to the net health outcomes of alternative intervention strategies, illustrated in the formula:

$$(C_1 - C_2)/(O_1 - O_2),$$

where C represents costs associated with an intervention, O represents outcomes, and 1 and 2 refer to alternative interventions. Costs associated with an intervention include the costs of the intervention itself plus those induced by the intervention (e.g., the costs of treating side effects), minus the costs averted because of the intervention (i.e., the costs of care for the prevented disease).

Outcomes in CEAs may be measured in different ways. Frequently, they are measured as life-years saved (LYS). While this measure accounts for how an intervention strategy affects mortality, it does not reflect the quality of life associated with different health outcomes. To capture the effect that intervention strategies have on both loss of and quality of life, the number of years with an illness or injury can be multiplied by a value weight from 0 (death) to 1 (full health) to generate quality-adjusted life-years (QALYs).[5] CEAs that use QALYs in the denominator of their cost-effectiveness ratios are often referred to as cost-utility analyses (CUAs), because they incorporate people's preferences, or utilities, for different states of health, illness, and injury. In our discussion, we treat CUAs as a subset of CEAs.

Economic analyses other than CEAs, such as cost-minimization analyses and cost-benefit analyses (CBAs), also provide information about the potential value of health services. CEAs differ from most of these types of analysis in that they describe how different strategies for allocating resources affect health outcomes.[4] For the third U.S. Preventive Services Task Force (USPSTF), this focus on health outcomes reflects an essential element of the approach to reviewing evidence. CBAs also incorporate health outcomes, but convert outcomes into dollars. Because assigning dollar values to health outcomes is controversial and not frequently used in U.S. health policy, the USPSTF has chosen to focus primarily on CEAs.

By quantifying the immediate and downstream benefits, harms, and costs of interventions, CEA demonstrates the trade-offs involved in choosing among different intervention strategies to effect desired health outcomes. As such, CEAs may provide valuable information for those designing or implementing policies about preventive services. In this paper, we discuss uses of CEA to guide policies related to clinical preventive services, some of the limitations in using CEA to inform recommendations for services, and the approach and methods the USPSTF is developing to systematically review CEAs and incorporate cost-effectiveness data into its process for developing recommendations for the forthcoming third edition of the *Guide to Clinical Preventive Services* (the *Guide*), slated for publication in 2003.

Table 1. Uses of cost effectiveness analysis in informing evidence-based recommendations for preventive services

(1)	Quantifying the differences between two or more effective services for the same condition
(2)	Illustrating the impact of delivering a given intervention at different intervals, different ages, or to different risk groups
(3)	Evaluating the potential role of new technologies
(4)	Identifying key conditions that must be met to achieve the intended benefit of an intervention
(5)	Incorporating preferences for intervention outcomes
(6)	Developing a ranking of services in order of their costs and expected benefits[a]

[a]The current U.S. Preventive Services Task Force will not use cost effectiveness analyses for this purpose.

Potential Uses of CEA in Informing Preventive Service Recommendations

Evidence-based recommendations are increasingly used to help determine which preventive and other services to include in clinical practice, public health programs, and benefits packages.[6,7] Most of these recommendations have not systematically incorporated evidence related to cost-effectiveness. CEAs, however, can be used in several ways to inform and extend clinical service recommendations (Table 1).

One of the most important and common uses of CEA is to examine the costs and health benefits associated with alternative interventions to achieve a given health outcome. For instance, effective screening strategies for colorectal cancer include fecal occult blood testing (FOBT),[8] sigmoidoscopy,[9] and possibly barium enema and colonoscopy.[10] More effective screening strategies often cost more than less effective strategies. Depending on available resources, some might screen initially with FOBT, which provides moderate effectiveness at relatively low cost, while others might choose colonoscopy, which is more costly but may also be more effective.[11–14] CEA makes explicit the trade-offs involved in these decisions.

CEAs can also help in selecting the most efficient application of effective interventions, such as the intervals between screening tests,[15,16] the ages for starting or stopping a service,[17] or the population subgroup likely to benefit most from a service.[18] Early detection of cervical neoplasia provides a pertinent example. In a CEA of cervical cancer screening, Eddy[15,16] demonstrated that Pap testing every 3 years saved 97% of the lives that would be saved using annual screening and

reduced costs by 67%. These results prompted several leading professional groups to issue a joint statement changing their recommendations to include triennial screening as a valid option.[16] Other CEAs have noted that screening women aged ≥65 who have had limited prior testing or are at high risk for cervical cancer can save both health care dollars and lives.[19] In contrast, screening low-risk women with a history of regular screening before age 65 increases the cost-effectiveness ratio more than tenfold over results for all women.[20] These results suggest that recommendations for screening older women for cervical cancer should be stratified according to risk of disease and prior screening history.

CEAs can also be used to evaluate new technologies related to prevention. For example, tests for mutations in the BRCA1 and BRCA2 genes, which confer high lifetime risks of developing breast and ovarian cancer,[21] can identify high-risk individuals, who can then be counseled about intensive surveillance for early disease detection or prophylactic surgery.[22,23] It is not clear, however, how such tests should be used in general practice. In this situation, one can model the costs and health consequences of using BRCA testing in different populations and calculate the marginal cost and effectiveness. For example, one could conduct a CEA to compare the cost effectiveness of screening all women versus screening only those with a strong family history of breast cancer. The results of such an analysis could help set policies about who should receive genetic testing and counseling.

CEAs can also help determine how factors that are not typically considered in clinical trials of intervention efficacy might influence the "real-world" effectiveness of a preventive service. For instance, there is evidence that doxycycline and azithromycin are equally efficacious in eradicating genital chlamydia infection in women.[24] It might seem reasonable to recommend doxycycline as the antibiotic of choice, since it is less expensive than azithromycin. However, when one considers that azithromycin is given as a single dose and is therefore associated with higher rates of adherence than doxycycline, azithromycin may in some settings improve outcomes compared with doxycycline and therefore be the more cost-effective choice.[25]

CEAs—more specifically, CUAs—can also be used to make explicit the impact of the target population's preferences for different health outcomes. By using QALYs as an outcome measure, CUAs account for the fact that most people prefer some states of health and illness to others. These preferences may need to be considered in deciding whether or not to implement a given preventive service. For instance, clinical trials typically report the effectiveness of tamoxifen in reducing overall morbidity and mortality as a balance between the benefits and harms of the drug, but fail to account for the different values that women place on various outcomes (e.g., breast cancer and endometrial cancer). In a CUA, the net effectiveness of the intervention is modeled as a weighted sum of benefits and harms, where the weights reflect women's preferences among these potential outcomes. Such information may be useful in establishing policies for large populations.

Finally, if CEAs are conducted in a standardized manner using the same units for measuring outcomes, preventive services can be ranked in a "league table," a listing of interventions in order of their costs of saving a year of life or QALY.[26–28] In a setting of limited resources, these methods for prioritizing services could be used as a guide in providing services for a population to maximize overall health for a given investment.

Overall, CEAs are a dynamic tool for developing and adapting effective preventive service interventions to obtain the best value for the greatest number of individuals at risk for poor health outcomes. However, they also have shortcomings. In the following section, we present a summary of limitations associated with using CEAs to inform evidence-based recommendations.

Limits of Using CEAs to Inform Preventive Service Recommendations

Prior USPSTFs and other groups have chosen not to incorporate cost effectiveness into their recommendations for several reasons, including a historical lack of standardized, high-quality CEAs; a paucity of CEAs for many preventive services; the questionable validity of QALYs in capturing preferences; a lack of transparency in the complex models used in many analyses; and concerns about the ethics and politics of rationing.

Until the last decade, there were few efforts in the United States to standardize the conduct of CEAs. As a result, many published analyses would not meet current criteria for high-quality CEA research.[29] Lack of standardization has made it difficult to compare studies about a specific preventive service or across different interventions.[30,31] In addition, for many services there has been a paucity of cost-effectiveness data, and for some services there are no economic evaluations at all.

Expanded use of QALYs as an outcome measure may improve the comparability of CEAs. Current use of QALYs, however, is limited by the shortcomings of existing preference measures, many of which are unvalidated and narrow in focus, not fully capturing the multifaceted nature of personal preference. QALYs as a measure are also not intuitively understood by most clinicians, policymakers, or patients. Moreover, results from a CEA using preferences of the general population to generate QALYs may not always be helpful to clinicians in their offices caring for individual patients with specific values that may differ from the average.

Using CEAs in making health decisions has also raised ethical concerns. CEAs typically assume that a

year of life saved or a QALY for an infant is equal to that for a 70-year-old, or that a gain of 1 year for one person is the same as a gain of a tenth of a year for ten people. These assumptions could be considered the least biased and a protection against discriminating against any group, but they may also inadequately reflect societal and individual values.[32–33]

Other ethical concerns relate to the use of CEA to ration health care services. Implicit in the use of CEAs in developing clinical recommendations is that societal health care resources are limited. In some industrialized countries this assumption, and the rationing of health care services, are made explicit. In the United States, CEAs have only rarely been used explicitly to set recommendations about services or funding levels. In the best-known case, the Oregon Health Services Commission ranked health care services according to their cost effectiveness, in order to expand health care coverage among low-income populations within the constrained Medicaid budget.[34] This approach was abandoned in the face of public criticism; many observers argued that rationing is not ethical, and that individuals should have access to all effective interventions.[35,36] Patients and health professionals alike expressed concern about the prospect of potentially valuable services being withheld to save money. In Oregon, cost effectiveness was ultimately used as one of several considerations in setting Medicaid-covered services. The Oregon experience illustrates that ranking services by their cost-effectiveness ratios may be a useful but not likely sufficient process for developing clinical service priorities. Most observers recognize that while CEAs are an important decision-making tool, they are not the only tool, and that many other factors, including ethical implications, public perceptions, and political and operational feasibility, need to be considered when prioritizing health care spending.

The perspective of a CEA—whose costs and benefits are considered in the analysis—is also important. A CEA using the societal perspective ideally incorporates an intervention's impact, in terms of costs and outcomes, on all members of society. If, however, an analysis is conducted from the perspective of a specific organization, such as a managed care provider, other costs (e.g., out-of-pocket patient costs and caregiver time) that are not relevant from the provider's perspective are not considered.[30] Such an analysis may be useful only to a select group of decision-makers. Moreover, because studies from varying perspectives assess different sets of costs and outcomes, they are not directly comparable. The Panel on Cost-Effectiveness in Health and Medicine[4] has recommended that all CEAs include the societal perspective. One limitation of this approach, however, is that the societal perspective may not reflect the specific concerns of some parties interested in using CEAs, such as individual practitioners, patients, or health care organizations. Another limitation is that enumerating all of the costs society experiences is often more difficult than quantifying those experienced by a specific entity, such as a health care system.

For these and other reasons, the USPSTF has, in the past, not used CEAs to inform its recommendations. Over the past several years, however, the quantity and quality of CEAs have increased substantially.[29] Theoretical refinement, methodologic advances, and the development of standards for reporting and conducting CEAs have improved their usefulness as decision-making tools. Moreover, as the cost of health care delivery has continued to rise, policymakers have found it increasingly difficult to decide about implementing clinical services solely on evidence of effectiveness, without consideration of costs. The third USPSTF has therefore decided to incorporate information from CEAs into its process for developing recommendations. While CEAs may never be able to address all of the complex issues involved in deciding how to allocate health care resources, their ability to quantify the trade-offs involved in choosing among different alternatives to improve health make them a valuable source of information in deciding which clinical preventive services to select and implement.

The USPSTF Approach

The USPSTF will conduct systematic reviews of CEAs to inform its recommendation process. These reviews will not replace the USPSTF's harms-benefits analyses and will not be conducted for every topic, but rather where relevant questions about cost effectiveness exist. Most of these questions will address the trade-offs between two or more effective strategies for achieving a given health outcome; the cost effectiveness of applying an intervention at varying intervals or to different target populations or risk groups; and the impact of factors such as adherence that may affect the costs and effectiveness of a given intervention. Examples of questions for which a CEA review might be initiated include the following: What is the cost-effectiveness of screening average-risk adults aged 20 to 30 for dyslipidemia? What is the comparative cost effectiveness of universal versus selective screening for chlamydial infection among women aged <25? What is the impact of varying levels of adherence on the cost effectiveness of colorectal cancer screening using sigmoidoscopy versus colonoscopy?

The USPSTF has set specific requirements for the use of CEAs in its recommendation process. First, there should be reasonable evidence that the intervention in question is effective. When definitive proof of effectiveness is difficult to achieve, the USPSTF may consider information from CEAs that make reasonable assumptions about the intervention's likely effectiveness. In general, however, the USPSTF will initiate a CEA review only for services where evidence of effectiveness exists.

Second, the USPSTF will use only economic analyses assessing the costs associated with achieving health outcomes. The results of studies that examine only intermediate measures, such as those reporting costs per patient screened or costs per case detected, are less interpretable in that the value of what is achieved for the costs accrued is less clear. These studies will therefore not be included in USPSTF CEA reviews.

Third, the USPSTF will focus primarily on CEAs that are conducted from the societal perspective. It will also give highest priority to studies in which valuations of outcomes, or QALYs, are derived from the perspective of general, rather than selected, populations.[4] In this manner, consistent with the USPSTF perspective, CEAs used in making decisions should reflect the public interest, and not be biased by any group that stands to gain or lose by the implementation of a particular preventive service.[26] Many CEAs include most but not all relevant costs accrued by society. Costs such as time and resources expended by patients and caregivers are frequently omitted. Such studies may nonetheless provide valuable information and will be considered. When reviewing these studies, the USPSTF will consider how including the relevant societal costs might have affected the studies' results.

Finally, the USPSTF will not create league tables to rank preventive services in order of cost effectiveness. Although the USPSTF strives to provide as much information as possible to guide decision-makers in their use of preventive services, a preliminary review of the cost effectiveness literature for several preventive services revealed that the quality and comparability of CEAs across services were not sufficient to allow direct comparisons and rankings. As standardization of methods and comparability of CEAs across preventive, diagnostic, and therapeutic services improves, future *Guides* may include league tables to allow for prioritizing services based on costs and expected benefits. In the meantime, *Partnership for Prevention*, a national nonprofit organization, has developed methods to estimate the relative value of services recommended by the second USPSTF to guide decision-makers in prioritizing effective preventive services.[37]

To sum up, CEAs are valuable decision-making tools that, when properly applied, can help maximize efficiency and appropriateness in health care delivery. The USPSTF recognizes that CEAs have limitations and that their use in informing health policies is controversial. It also recognizes, however, that users of the third *Guide*, if not provided with information from CEAs, are still likely to use economic analyses, potentially in an unsystematic way. The USPSTF will therefore attempt to provide unbiased summaries of cost-effectiveness data where relevant, based on a systematic approach to, and critical appraisal of, the literature. In circumstances where information on cost-effectiveness is unavailable but is felt to be vital to the shaping of a recommendation, the USPSTF may conduct an original CEA.

Methods to Review CEAs to Inform Recommendations for Preventive Services

Conceptual Approach

Systematically reviewing CEAs shares much in common with the process for reviewing studies of intervention effectiveness.[38] The goal in both cases is to identify the best available evidence regarding a specific question and to critically review and synthesize that evidence in order to answer the question in an evidence-based way. However, reviewing CEAs is also fundamentally different from reviewing effectiveness studies. For example, in a systematic review of the effectiveness of a single intervention, the effect sizes from several clinical trials, which represent unique samples of data gathered in a similar fashion, might be pooled in order to obtain a more accurate estimate of the intervention's effectiveness. It is difficult, however, to combine the results of several CEAs into a single cost-effectiveness ratio, because they often do not involve primary data collection and are frequently based on assumptions and models that vary in a way that may make combining results from multiple studies difficult or conceptually unsound. In addition, while the USPSTF's systematic reviews of intervention effectiveness involve developing an analytic framework of the various components of effectiveness and critically appraising the literature related to each component separately,[38] CEAs typically use decision analytic modeling to include all the components of such a framework in a single study.

Why then, conduct a systematic review of CEAs rather than identify a single study that addresses the question at hand? CEAs vary widely in their methods and assumptions. Because of this variation, systematically reviewing CEAs provides several benefits. First, because CEAs draw on a variety of cost and effectiveness data sources to develop input parameters, a systematic review can identify which analyses use the best available evidence for key inputs and are therefore the most evidence based. Second, because the credibility of CEAs rests on their quality, a critical review of CEAs and a rating of the quality of each allow for identifying the most methodologically rigorous studies. Third, a comprehensive review can identify the studies that best address the question being asked. Fourth, comparatively assessing CEAs can help to identify variables and methods that significantly influence the estimated benefits and cost effectiveness of an intervention. For instance, some CEAs might assume no harms from a given intervention, while others might assume that the intervention has significant harms. Comparing these studies side by side may provide insight into how the assumption or lack of assumption of harm affects the

estimated benefit of the intervention. While some assumptions are varied within a single study using sensitivity analysis, most CEAs provide a limited number of sensitivity analyses. Thus, systematically reviewing CEAs may help identify, through a side-by-side comparison that amounts to a "virtual sensitivity analysis," the impact of different assumptions on the benefits of a given intervention. Finally, the more high-quality, independently conducted CEAs there are for a given intervention, the more convincing the evidence.

Developing the Instrument and Process for Abstracting Data

To systematically review CEAs, we first developed a tool for abstracting relevant information from individual studies in a standardized way. Through a literature search and consultation with experts, we located several existing abstraction tools[28,39] and quality-rating criteria.[4,40,41] We drew on the strengths of each of these instruments to develop a novel abstraction tool that met the needs and objectives of the USPSTF. The tool is largely adapted from the CEA abstraction instruments developed by the Task Force on Community Preventive Services[39] and the Harvard Center for Risk Analysis.[29]

The USPSTF CEA abstraction instrument, which we are currently piloting, was designed to (1) ensure that the CEAs being reviewed are applicable to the question posed, (2) assess the studies' methodological rigor, (3) ascertain that their models contain the appropriate components of effectiveness, (4) examine the degree to which they use the best available evidence of effectiveness, (5) evaluate the validity and impact of their assumptions, and (6) assess the type and quality of cost information used. Our criteria for rating methodological quality are based on recommendations of the Panel on Cost-Effectiveness in Health and Medicine.[4] Sample quality rating items are listed in Table 2. Because simple counts of criteria fulfilled do not differentiate studies of varying quality with great precision, these criteria will not be used to generate quality scores but rather as a guide in categorizing study quality as high, fair, or poor.

Our reviews will focus mainly on high-quality studies. When few or no high-quality studies exist for a given question, we will also consider studies rated fair. Poor-quality studies will not be considered. Our objective is to present the best evidence currently available while appropriately identifying study limitations, because policymakers are sometimes required to make decisions without having perfect information.

Process for Reviewing Studies

The process for systematically reviewing CEAs is similar to that for reviewing studies of effectiveness (Table 3).

Table 2. Sample quality rating items for cost effectiveness analyses

Framing
Are the interventions and populations compared appropriate?
Is the study conducted from the societal perspective?
Is the time horizon clinically appropriate and relevant to the study question?
Effects
Are all important drivers of effectiveness included?
Are key harms included?
Is the best available evidence used to estimate effectiveness?
Are long-term outcomes used?
Do effect measures capture preferences or utilities?
Costs
Are all appropriate downstream medical costs included?
Are charges converted to costs appropriately?
Are the best available data used to estimate costs?
Results
Are incremental cost-effectiveness ratios presented?
Are appropriate sensitivity analyses performed?

As with any systematic review, before reviewing the evidence, one must define the question at hand. USPSTF "topic teams"[38] reviewing the evidence for the effectiveness of preventive services within specific clinical topics (e.g., screening for hypertension) are asked to identify relevant questions related to the cost effectiveness of services within each topic (Table 1).

Once the question is identified, a comprehensive search for appropriate CEAs is conducted. Searches may be limited by year (e.g., after 1990), based on when relevant technologies came into use. Abstracts identified by the search are screened for inclusion using three items: (1) Does the study address the identified question? (2) Is the study an original CEA? (3) Does the study report results using an appropriate outcome metric (e.g., LYS, QALY, or cases of illness averted)?. If no CEAs exist for a specific question, we consider reviewing other types of economic analyses, such as CBAs.

Studies meeting inclusion criteria are abstracted by at least two reviewers. To determine whether the best available evidence was used in each study, whether included assumptions are reasonable, and whether

Table 3. U.S. Preventive Services Task Force process for conducting a systematic review of cost-effectiveness analyses

(1) Define the question to be addressed.
(2) Comprehensively search relevant literature databases.
(3) Screen abstracts for inclusion.
(4) Review reference lists and call experts to identify studies not captured by the literature search.
(5) Abstract relevant studies.
(6) Compare the impact of varying assumptions and resolve differential results across studies through consensus.
(7) Synthesize and present results in evidence tables.

each study appropriately addresses the question at hand, the CEA review team for each question includes a member of the topic team reviewing the effectiveness evidence for that topic.[38] The data used in the CEA are compared with the evidence derived from the systematic review of effectiveness conducted by the topic team, which serves as the "gold standard" for whether the best available evidence was used.

After abstracting studies, reviewers discuss how studies differ in their assumptions, how varying assumptions affect study results, and how different studies may arrive at different conclusions. Finally, key information addressing the initial question and highlighting study quality and the effect of various assumptions are summarized in evidence tables.

Conclusions

CEAs are valuable tools for incorporating cost considerations into evidence-based clinical decisions. This article has outlined the USPSTF's strategy to incorporate information from CEAs into its process for recommending clinical preventive services. Through these efforts, we hope not only to provide guidance about implementing preventive services, but to identify unmet needs in economic analyses of preventive health care, illuminate some of the trade-offs in alternative approaches to delivering preventive services, and provide substrata for policy discussions and public debate over the role of cost effectiveness in allocating health care resources.

In the future, ranking of preventive services based on cost effectiveness may provide busy clinicians and their patients with some scientific basis for deciding how to best spend their limited time providing or carrying out the services that are most likely to have the greatest impact on health. At present, CEAs should be considered an important aid to decision makers striving to achieve the best possible health for a population.

Supported by contract #290-97-0018 (Task Order #2) to the Oregon Health Sciences University (SS, MH) and contract #290-97-0011 (Task Order #3) to the Research Triangle Institute/University of North Carolina (TJH, MP) from the Agency for Healthcare Research and Quality, and contract # DAMD17-94-J-4212 from the Department of the Army (JSM). The views expressed in this article are those of the authors and do not necessarily reflect those of the Agency for Healthcare Research and Quality or the Department of the Army.

We thank Vilma G. Carande-Kulis, MS, PhD; Joanna E. Siegel, ScD, RN; Dennis G. Fryback, PhD; Milton J. Weinstein, PhD; and the members of the third U.S. Preventive Services Task Force, for comments on earlier versions of this manuscript; the *Partnership for Prevention* Committee on Clinical Preventive Service Priorities and Peter J. Neumann, ScD, for sharing their work; and Kathryn Pyle Krages, AMLS, MA, Susan Wingenfeld, and Gary Miranda, MA, for administrative support and help with manuscript preparation and editing.

References

1. Levit K, Cowan C, Lazenby H, et al. Health spending in 1998: signals of change. The Health Accounts Team. Health Affairs 2000;19:124–32.
2. Weinstein MJ, Garber AM, Fryback DG. Disease Prevention Research at NIH: An Agenda for All. Workshop J: Prevention strategies, economic realities, and identification of prevention research needs. Prev Med 1994; 23:571–2.
3. Teutsch SM, Murray JF. Dissecting cost-effectiveness analysis for preventive interventions: a guide for decision makers. Am J Manag Care 1999;5:301–5.
4. Gold M, Seigel J, Russell L, Weinstein MC. Cost-effectiveness in health and medicine. New York: Oxford University Press, 1996.
5. Gold MR, Patrick DL, Torrance GW, et al. Identifying and valuing outcomes. In: Gold M, Seigel J, Russell L, Weinstein MC, eds. Cost-effectiveness in health and medicine. New York: Oxford University Press, 1996:82–134.
6. Kattlove H, Liberati A, Keeler E, Brook RH. Benefits and costs of screening and treatment for early breast cancer: development of a basic benefit package. JAMA 1995;273:142–8.
7. Prosser LA, Koplan JP, Neumann PJ, Weinstein MC. Barriers to using cost-effectiveness analysis in managed care decision making. Am J Manag Care 2000;6:173–9.
8. Mandel JS, Bond JH, Church TR, et al. Reducing mortality from colorectal cancer by screening for fecal occult blood: Minnesota Colon Cancer Control Study. New Eng J Med 1993;328:1365–71 (published erratum appears in N Engl J Med 1993 Aug 26;329[9]:672).
9. Selby JV, Friedman GD, Quesenberry CP Jr, Weiss NS. A case-control study of screening sigmoidoscopy and mortality from colorectal cancer. New Eng J Med 1992;326:653–7.
10. Winawer SJ, Fletcher RH, Miller L, et al. Colorectal cancer screening: clinical guidelines and rationale. Gastroenterology 1997;112:594–642 (published errata appear in Gastroenterology 1997;112[3]:1060 and 1998; 114[3]:625).
11. Eddy DM. Screening for colorectal cancer. Ann Intern Med 1990;113:373–84.
12. Frazier AL, Colditz GA, Fuchs CS, Kuntz KM. Cost-effectiveness of screening for colorectal cancer in the general population. JAMA 2000;284:1954–61.
13. Khandker RK, Dulski JD, Kilpatrick JB, Ellis RP, Mitchell JB, Baine WB. A decision model and cost-effectiveness analysis of colorectal cancer screening and surveillance guidelines for average-risk adults. Int J Technol Assess Health Care 2000;16:799–810.
14. Wagner JL, Tunis S, Brown M, Ching A, Almeida R. Cost-effectiveness of colorectal cancer screening in average-risk adults. In: Young GP, Rozen P, Levin B, eds. Prevention and early detection of colorectal cancer. Philadelphia: W.B. Saunders, 1996:321–56.
15 Eddy DM. Screening for cervical cancer. Ann Intern Med 1990;113:214–26.
16. Eddy DM. Screening for cervical cancer: common screening tests. Philadelphia: American College of Physicians, 1991.
17. Kerlikowske K, Salzmann P, Phillips KA, Cauley JA, Cummings SR. Continuing screening mammography in women aged 70 to 79 years: impact on life expectancy and cost-effectiveness. JAMA 1999;282:2156–63.
18. Prosser LA, Stinnett AA, Goldman PA, et al. Cost-effectiveness of cholesterol-lowering therapies according to selected patient characteristics. Ann Intern Med 2000;132:769–79.
19. Mandelblatt JS, Fahs MC. The cost-effectiveness of cervical cancer screening for low-income elderly women. JAMA 1988;259:2409–13.
20. Fahs MC, Mandelblatt J, Schechter C, Muller C. Cost effectiveness of cervical cancer screening for the elderly. Ann Intern Med 1992;117:520–7.
21. Ford D, Easton DF, Stratton M, et al. Genetic heterogeneity and penetrance analysis of the BRCA1 and BRCA2 genes in breast cancer families: the Breast Cancer Linkage Consortium. Am J Hum Genet 1998;62:676–89.
22. Burke W, Daly M, Garber J, et al. Recommendations for follow-up care of individuals with an inherited predisposition to cancer. II. BRCA1 and BRCA2. Cancer Genetics Studies Consortium. JAMA 1997;277:997–1003.
23. Schrag D, Kuntz KM, Garber JE, Weeks JC. Benefit of prophylactic mastectomy for women with BRCA1 or BRCA2 mutations. JAMA 2000;283: 3070–2.
24. Martin DH, Mroczkowski TF, Dalu ZA, et al. A controlled trial of a single dose of azithromycin for the treatment of chlamydial urethritis and

cervicitis. The Azithromycin for Chlamydial Infections Study Group. New Eng J Med 1992;327:921–5.
25. Genc M, Mardh A. A cost-effectiveness analysis of screening and treatment for Chlamydia trachomatis infection in asymptomatic women. Ann Intern Med 1996;124:1–7.
26. Russell LB, Siegel JE, Daniels N, Gold MR, Luce BR, Mandelblatt J. Cost-effectiveness analysis as a guide to resource allocation in health: roles and limitations. In: Gold M, Seigel J, Russell L, Weinstein MC, eds. Cost-effectiveness in health and medicine. New York: Oxford University Press, 1996:3–24.
27. Drummond M, Torrance G, Mason J. Cost-effectiveness league tables: more harm than good? Soc Sci Med 1993;37:33–40.
28. Stone PW, Teutsch SM, Chapman RH, Bell C, Goldie SJ, Neumann PJ. Cost-utility analyses of clinical preventive services: published ratios, 1976–1997. Am J Prev Med 2000;19:15–23.
29. Neumann PJ, Stone PW, Chapman RH, Sandberg EA, Bell CM. The quality of reporting in published cost-utility analyses, 1976–1997. Ann Intern Med 2000;132:964–72.
30. Russell LB, Gold MR, Siegel JE, Daniels N, Weinstein MC. The role of cost-effectiveness analysis in health and medicine. Panel on Cost-Effectiveness in Health and Medicine. JAMA 1996;276:1172–7.
31. Brown ML, Fintor L. Cost-effectiveness of breast cancer screening: preliminary results of a systematic review of the literature. Breast Cancer Res Treat 1993;25:113–8.
32. Ubel PA, Nord E, Gold M, Menzel P, Prades JL, Richardson J. Improving value measurement in cost-effectiveness analysis. Med Care 2000;38:892–901.
33. Daniels N. Rationing fairly: programmatic considerations. Bioethics 1993; 7:223–33.
34. Klevit HD, Bates AC, Castanares T, Kirk EP, Sipes-Metzler PR, Wopat R. Prioritization of health care services: a progress report by the Oregon Health Services Commission. Arch Intern Med 1991;151:912–6.
35. Hadorn DC. Setting health care priorities in Oregon: cost-effectiveness meets the rule of rescue. JAMA 1991;265:2218–25.
36. Brown LD. The national politics of Oregon's rationing plan. Health Affairs 1991;10:28–51.
37. Coffield AB, Maciosek MV, McGinnis JM, et al. Priorities among recommended clinical preventive services. Am J Prev Med 2001. In press.
38. Harris RP, Helfand M, Woolf SH, et al. Current methods of the U.S. Preventive Services Task Force: a review of the process. Am J Prev Med: 2001;20(suppl 3):21–35.
39. Carande-Kulis VG, Maciosek MV, Briss PA, et al. Methods for systematic reviews of economic evaluations for the Guide to Community Preventive Services. Task Force on Community Preventive Services. Am J Prev Med 2000;18:75–91.
40. Drummond MF, Jefferson TO. Guidelines for authors and peer reviewers of economic submissions to the BMJ. Br Med J 1996;313:275–83.
41. Udvarhelyi IS, Colditz GA, Rai A, Epstein AM. Cost-effectiveness and cost-benefit analyses in the medical literature. Are the methods being used correctly? Ann Intern Med 1992;116:238–44.